

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of)

BOYMOND et al.)

Serial No. 09/647,069)

Filed: September 26, 2000)

For: PROCESS FOR PREPARING GRIGNARD COMPOUNDS)

Art Unit: 1627

Examiner: Epperson

#1627
3/10/03
10-18-03

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BRIEF ON APPEAL

Sir:

Pursuant to the Notice of Appeal filed on August 5, 2003, appellants present
herewith their Brief on Appeal from the examiner's final rejection mailed on March 5,
2003.

REAL PARTY IN INTEREST

The real party in interest is BASF Aktiengesellschaft of Ludwigshafen, Germany.

RELATED APPEALS AND INTERFERENCES

To the best of the undersigned's knowledge, there are no related appeals or interferences within the meaning of 37 CFR §1.192(c)(2).

STATUS OF CLAIMS

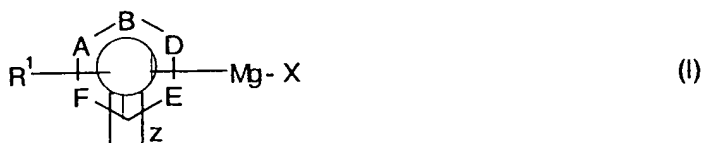
Claims 1-4 are pending in the instant case. Claims 5-8 has been canceled.

STATUS OF AMENDMENTS

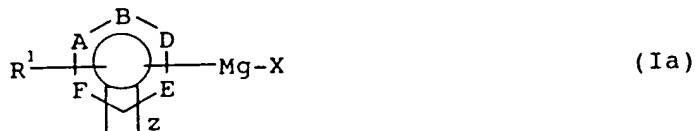
An amendment filed under 37 CFR 1.116 is filed herewith in order to cancel the non-elected claims and place the application in better condition for appeal.

SUMMARY OF INVENTION

The invention relates to a process of preparing Grignard compounds of the formula I



The invention additionally relates to the compounds of formula I and polymer-bound compounds of the formula Ia



ISSUES

The issue presented for review by the Board of Patent Appeals and Interferences is:

Whether claims 1-4 are unpatentable under 35 USC §103 as unpatentable over Ohno et al., (US 5,420,310), in view of Minoura et al. (J. Polym.Sci., Part A-1, 1969, 7(11), 3245-55) and Capporiccio et al (US 4,254,030).

GROUPING OF CLAIMS

As the issue above applies to all of the claims, the claims stand or fall together.

ARGUMENT

The examiner has rejected under 35 USC 103(a) as unpatentable over Ohno in view of Minoura (J. Polym. Sci., Part A-1, 1969, 7(11), 3245-55) and Capporiccio (US 4,354,030).

The examiner argues that Ohno teaches the magnesium-halogen exchange reaction as the applicant, except that Ohno lacks the teaching of carrying out the magnesium-halogen exchange reaction on a solid support. The examiner goes on to state that the solid support step is disclosed by the Minoura reference and that Caporiccio teaches the synthetic usefulness of performing a magnesium-halogen exchange reaction on a solid support using copolymers of fluorosulphonyl olefins. (Page 8 of the Office action dated June 19, 2002).

The examiner suggests that it would be *prima facie* obvious to one of ordinary skill in the art to carry out the magnesium-halogen exchange reaction of Ohno on the

polyvinyl chloride solid support of Minoura because Caporiccio suggests that higher yields may be obtained. However, three requirements must be fulfilled in order for a *prima facie* case of obviousness to be satisfied. First, there must be some suggestion or motivation in the references themselves or available to one of ordinary skill in the art to modify the reference or to combine reference teachings.¹ Second, there must be a reasonable expectation of success. Third, the prior art references combined must teach or suggest all the claim limitations. MPEP §2143.

The claimed invention must be considered as a whole, the references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination, the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention and reasonable expectation of success is the standard with which obviousness is determined. MPEP §2141, citing *Hodosh v. Block Drug Co., Inc.* 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).

With respect to the instant invention, the examiner has failed to establish a *prima facie* case of obviousness. The references cited by the examiner do not provide a suggestion or motivation to combine the teachings to produce the instant invention. As noted above, the examiner suggests that one of ordinary skill in the art would have been motivated to produce the instant invention because Caporiccio suggests that

¹There are three possible sources for motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art. *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-1458 (Fed. Cir. 1988).

higher yields may be obtained.

However, this citation that higher yields may be obtained refers to a process that does not produce compounds of the formula I, nor does it involve compounds of the formula II. Furthermore, a single line in a reference should not be taken out of context and relied upon with the benefit of hindsight to show obviousness. *Bausch & Lomb, Inc. V. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 230 USPQ 416 (Fed. Cir. 1986). That is, the examiner utilizes the statement that higher yields are obtained in Caporiccio to support the obviousness rejection in the instant invention which produces different materials than that of Caporiccio. Caporiccio discusses fluorosulphonyloxafluoroalkanes and their reactions with Grignard compounds. In contrast to that of Caporiccio, the instant invention produces the five or six-membered residue as claimed in claim 1, formula 1.

In response to these remarks the examiner argues further

The Examiner's position here is that the above 35 USC §103 rejection has not used references "out of context" as suggest by applicant not applied an "obvious to try" test. [sic] Here, applicants have stated that the Examiner cited the references "out of context", but applicants have not provided any basis (i.e., no scientific reasoning) for making such a a statement. Furthermore, applicants have not show [sic] what "alternative" context they believe these references are made under.

Office Action dated March 5, 2003, page 7.

These remarks appear to misconstrue the argument that applicants set forth in the office action of December 19, 2002. *Bausch & Lomb*, cited above, merely states that a single line in a reference should not be taken out of context and relied upon, not

that “the Examiner cited the references “out of context.” Furthermore, the examiner argues that it is improper for the applicant to attack the references individually. While the obviousness rejection itself is based on a number of references, the examiner relies only on Caporricio to supply the requisite motivation to support a *prima facie* case of obviousness and thus applicants comments are directed solely to this reference in support of this element of the obviousness rejection.

Utilizing the general statement that Caporricio suggests that higher yields may be obtained the examiner seems to utilize an “obvious to try” standard of invention. However this is not the standard of invention under 35 USC §103. “Obvious to try” is not a valid test of patentability. *In re Dow Chemical Company*, 5 USPQ2d 1529, 1532 (Fed. Cir. 1988). A general statement that one reaction produces higher yields cannot supply the motivation to combine references. This argument is similar to a case in which the Federal Circuit found that no suggestion to modify the prior art existed. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), cited in the MPEP at §2143.01. The MPEP states,

In, *In re Fine*, the claims were directed to a system for detecting and measuring minute quantities on nitrogen compounds comprising a gas chromatograph, a converter which converts nitrogen compounds into nitric oxide by combustion, and a nitric oxide detector. The primary reference disclosed a system for monitoring sulfur compounds comprising a chromatograph, combustion means, and a detector, and the secondary reference taught nitric oxide detectors. The examiner and Board asserted that it would have been within the skill of the art to substitute one type of detector for another in the system of the primary reference, however the court found there was no support or explanation of this conclusion and reversed.

Similar to *Fine*, the examiner in the instant case suggests that substituting one reaction for another on a solid support would have been obvious to one of ordinary skill in the art. Indeed, the examiner explicitly states that a “motivation for cleaner products and higher yields was well known to those of skill in the art at the time of filing for performing any solution based organic chemistry reaction on a solid-support (i.e., a person of skill in the art would always have been motivated to perform any solution based organic reaction on a solid-support to increase purity and yield).” Office action of March 5, 2003, page 6. However, we can see from *Fine* that this does not meet the standard of obviousness in view of the Federal Circuit.

Second, the examiner has failed to show that the applicants had an expectation of success. The examiner argues that applicants had an expectation of success of the claimed invention as “both Minoura et al and Caproiccio et al teach that magnesium-halogen exchange reactions can occur for reactions involving alkyl halides on a solid support.” (Paper number 10, page 9). However, these references do not suggest the success of the instant invention. As discussed before, the examiner seems to import an “obvious to try” standard as the standard for obviousness. According to the Federal Circuit this is not the correct standard.

In *In re Roemer*, the Federal Circuit found that a reference amounted to an “obvious to try” suggestion where the reference provided only general guidance as to the particular form of the claimed invention or how to achieve it. 59 USPQ2d 1527, 1531 (Fed. Cir. 2001). Citing *In re O’Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673,1681

(1988) and *In re Deuel*, 51 F.3d 1552, 1559, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995).

In fact, in this instance, the examiner does not cite the general guidance in any of the references to combine them to produce the instant invention, but merely relies on the general statement that purer yields may be obtained. The examiner requires one of ordinary skill in the art to infer that the claimed process would be successful when these three references are presented together and also to know how to carry this out.

In further support of this argument the examiner argues that the Grignard reactions are well known since the early 1900's and the mechanism of reaction is well established. However, this appears to ignore the literature that outlines the difficulty of obtaining the instant invention. For example, the inventors report that very few functionalized organomagnesium reagents have been prepared due to the low functional-group tolerance of these reagents. Preparation of Highly Functionalized Grignard Reagents by an Iodine-Magnesium Exchange Reaction and its Application in Solid-Phase Synthesis, *Angew. Chem. Int. Ed.* 1998. 37 No. 12. Furthermore, the inventors state in the specification that the drastic conditions of the procedures under the prior art do not permit other functional groups, such as ester or nitrile moieties, which are able to react with a Grignard compound as electrophile to be retained in the molecule, because oligomerization, reduction or other side reactions would occur. Specification p. 2. Furthermore, the prior art references combined do not teach or suggest all the claim limitations together.

In effect the examiner has chosen to combine these three references with the

hindsight of the applicants specification. However, one cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Taken as a whole the references do not provide the motivation to one of ordinary skill in the art to produce the claimed invention nor does one of ordinary skill in the art have an expectation of success from the cited references. Therefore, applicants respectfully assert that a *prima facie* case of obviousness has not been established.

Alternatively, even if a *prima facie* case of obviousness has been established applicants have overcome this showing with the showing of unexpected results. Proof of an unexpected improvement may rebut a *prima facie* case of obviousness. *In re Murch*, 464 F.2d 1051, 175 USPQ 89 (CCPA 1972). Indeed, it is always error to exclude evidence of secondary indicators. *Stratoflex v. Aeroquip Corp.*, 713 F.2d 1540, 218 USPQ 871 (Fed. Cir. 1983). Data to support this improvement is set forth in applicant's specification in Tables I and II. The results as set forth in Table II produced a yield of free product of usually 90% or more. Applicant's specification p. 16, 17-19.

CONCLUSION

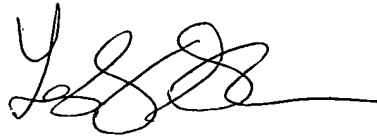
In view of the above remarks applicants respectfully request the examiner's decision be reversed.

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees to Deposit Account No. 11-0345. Please credit

any excess fees to such deposit account.

Respectfully submitted,

KEIL & WEINKAUF

A handwritten signature in black ink, appearing to read 'LESLEY E. SHAW', with a long horizontal flourish extending to the right.

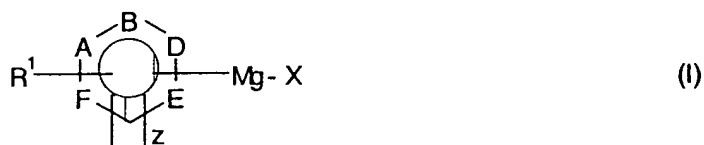
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APPENDIX

1. A process for preparing compounds of the general formula I



which comprises reacting compounds of the general formula II



with compounds of the formula R^4MgX (III) at temperatures below 0°C , where the substituents and variables in the formulae, I, II and III have the following meanings:

wherein Z is 0 or 1

wherein X is halogen or R^2

wherein X^a is Br, or I

wherein A, B, D and E

independently of one another are CH, CR^2 , N, P or CR^3 wherein F is O, S,

NR^6 , CR^2 , or CR^3 when $z = 0$, or CH, CR^2 , N, P or CR^3 when $z = 1$,

wherein two adjacent variables A, B, D, E or F together optionally form another substituted or unsubstituted aromatic saturated or partially saturated ring which has 5 to 8 atoms in the ring and which may contain one or more heteroatoms

such as O, N, S, P, and not more than three of the variables, A, B, D, E or F
being a heteroatom,

wherein R^1 is $COOR^2$, CN, $CONR^3R^3'$, or Halogen

wherein R^2 is substituted or unsubstituted, branched or unbranched C_1 - C_{10} -alkyl,
 C_3 - C_{10} -cycloalkyl, C_1 - C_4 -alkylaryl, C_1 - C_4 -alkylhetaryl, or R^5 ,

wherein R^3 is hydrogen, substituted or unsubstituted, branched or unbranched
- OC_1 - C_{10} -alkyl, - OC_3 - C_{10} -cycloalkyl, - OC_1 - C_4 -alkylaryl, - OC_1 - C_4 -alkylhetaryl,
 R^3' or R^5 ,

wherein R^3' is hydrogen, substituted or unsubstituted, branched or unbranched
 C_1 - C_{10} -alkyl, C_3 - C_{10} -cycloalkyl, C_1 - C_4 -alkylaryl, C_1 - C_4 -alkylhetaryl, or R^5 ,

wherein R^4 is substituted or unsubstituted, branched or unbranched C_1 - C_{10} -alkyl,
 C_3 - C_{10} -cycloalkyl, C_1 - C_4 -alkylaryl, C_1 - C_4 -alkylhetaryl, or halogen,

wherein R^5 is a solid support,

wherein R^6 is substituted or unsubstituted, branched or unbranched C_1 - C_{10} -alkyl,
 C_3 - C_{10} -cycloalkyl, C_1 - C_4 -alkylaryl, C_1 - C_4 -alkylhetaryl, substituted or
unsubstituted, branched or unbranched $-(C=O)-C_1$ - C_{10} -alkyl, $-(C=O)-C_3$ -
 C_{10} -cycloalkyl, $-(C=O)-C_1$ - C_4 -alkylaryl, $-(C=O)-C_1$ - C_4 -alkylhetaryl or $-SO_2$ -
aryl

where the process is carried out on a solid support (R^5).

2. A process as claimed in claim 1, which is carried out in an inert aprotic solvent.
3. A process as claimed in claim 1, which is carried out at temperatures below -

15°C.

4. A process as claimed in claim 1, wherein the reaction to give compounds of the formula I as set forth in claim 1 is complete within 10 hours.